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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,060	06/10/2003	L. Gordon Letts	102258.157US1	8895
25270	7590	03/31/2006	EXAMINER	
EDWARD D GRIEFF HALE & DORR LLP 1455 PENNSYLVANIA AVE, NW WASHINGTON, DC 20004			ANDERSON, REBECCA L	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,060	LETTS ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12 January 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-81 is/are pending in the application.
- 4a) Of the above claim(s) 3-52 and 56-81 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 2 and 53 is/are rejected.
- 7) Claim(s) 1, 2 and 53-55 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/05 and 3/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Claims 1-81 are currently pending in the instant application. Claims 3-52 and 56-81 are withdrawn from consideration as being for non-elected subject matter, claims 1, 2 and 53-55 are objected and claims 1, 2 and 53 are rejected.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2 and 53-55 and the further election of the compound of formula IV in the reply filed on 12 January 2006 is acknowledged. The traversal is on the ground(s) that restriction is not proper when the claims are related and the examiner has not shown either that there is a separate classification of the claims; a separate status in the art or a different field of search.

Applicant also argues that a search of the prior art for one group would necessarily encompass a search of the prior art for additional groups and applicant proposes a restriction with three groups. This is not found persuasive because the separate classification of the claims is seen in the restriction requirement on pages 3-5 wherein the various classification of the groups is found, for example, in class 514, 544, 546, 548, 549, 514, 435, 562, etc. The different field of search is found on page 11 wherein the plethora of classes and subclasses in each of the groups imposes a serious burden on the examiner to perform a complete search of the defined areas and wherein a search for one group is not required for another group. Furthermore, in regards to applicants' search argument, the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent

subject matter which require different searching strategies for each group.. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Therefore, as stated on pages 6 and 7 of the previous restriction requirement, **the elected invention for search and examination is:** the compounds and pharmaceutical compositions of the formula (I) wherein:

R5, R6, R7, R8, R9, R4 and K are as defined in claim 1;

X is an oxygen; and

T is an oxygen.

The elected invention for search and examination includes the compounds of the formulas II, IV, III, VI, VII and VIII.

The remaining subject matter of claims 1, 2 and 53-55 that is not drawn to the above elected invention and the subject matter of claims 3-52 and 56-81 stands withdrawn under 37 CFR 1.142(b) as being for non-elected subject matter. The remaining compounds which are not within the elected invention, which are independent and distinct from the elected invention and do not have unity with the elected compound and are therefore withdrawn by means of a restriction requirement within the claims are, for example, the compounds of formulas V, IX, X, XI, XII, XIII, XIV, XV, XVI, XVII (which either include nitroxyl lower alkyl esters or do not contain at least one –NO group or at least one –NO₂ group) and the compounds of the formula (I) wherein, for example, X is –S(O)o- or -N(Ra)Ri- and/or T is a covalent bond, a carbonyl, -S(O)o- or -N(Ra)Ri-.

The above mentioned withdrawn compounds, which are withdrawn from consideration as being for nonelected subject matter, differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds differ from those of the elected invention, such as by carboxamide or a thiocarboxylate ester, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the compounds can be seen by the various classification of these compounds in the U.S. classification system, i.e. class 560/49+ carboxylic acid esters, class 558/230+ thiocarboxylate esters, class 564/123+ carboxamide, etc. Therefore, again, the compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter.

These withdrawn compounds are independent and distinct from the elected invention and do not have unity with the compound elected and are therefor withdrawn by means of a restriction requirement within the claims.

The requirement is still deemed proper.

Claim Objections

Claims 1, 2 and 53-55 are objected to as containing non-elected subject matter. Claims 1, 2 and 53-55 presented drawn solely to the elected invention identified supra as: the elected invention for search and examination, would overcome this objection.

Claims 54 and 55 are also objected to as being dependent upon a rejected base claim, but would appear allowable if rewritten in independent form including all of the

limitations of the base claim and any intervening claims and presented drawn solely to the elected invention as identified supra.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

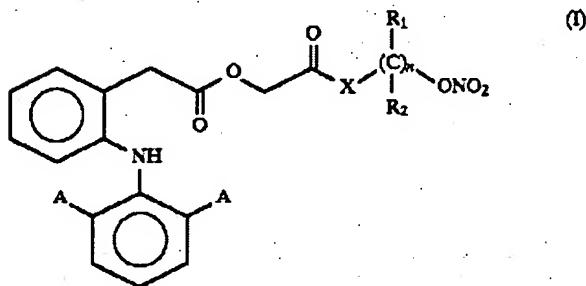
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,844,696 (SERRA).

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Determining the scope and contents of the prior art

SERRA discloses the compounds of the formula (I) on column 1:



where:

A is fluorine, chlorine or bromine;

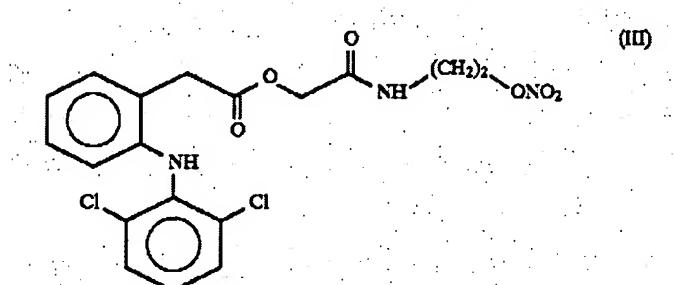
X means oxygen, NH or NR where R means a linear or branched alkyl chain of 1 to 6 carbon atoms;

R₁ and R₂ mean, independently, hydrogen or a linear or branched alkyl chain of 1 to 6 carbon atoms; and

and n is a number between 1 to 10.

These compounds are useful as anti-inflammatory and analgesic agents (see column

1). Column 2 further discloses the compound of the formula III:



While compounds wherein one A is fluorine is not specifically named, as seen in formula III wherein both A's are disclosed as Cl, and it is necessary to select portions of teachings within the reference and combine them, the compounds are still considered obvious because the substituents are sufficiently limited and well delineated, i.e. each A is either fluorine, chlorine or bromine. One of ordinary skill in the art is able to "at once envisage" the specific

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compound within the generic chemical formula wherein one of A is fluorine and one is chlorine.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of SERRA.

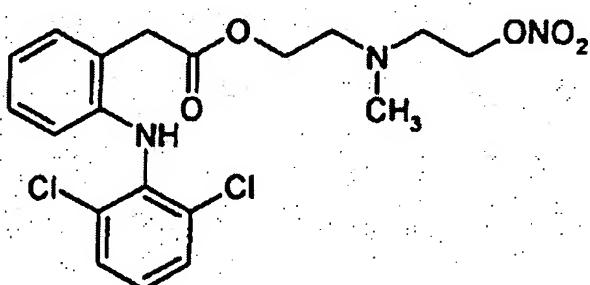
SERRA discloses the compounds of formula I and III which are useful as anti-inflammatory and analgesic agents, which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been

motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato (WO 2001012584).

Determining the scope and contents of the prior art

Del Soldato discloses compounds of the formula A-B-N(O)s (page 6) which are useful for, such as, anti-inflammatory agents (page 2). Specific compounds of formula A-B-N(O)s are disclosed, such as, the formula of example 14, page 49:



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected

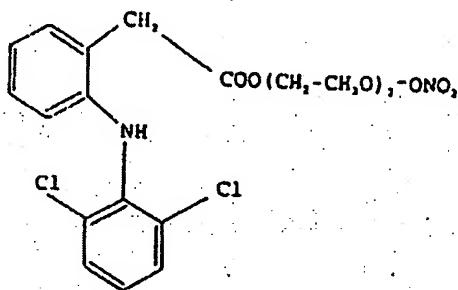
invention wherein R4 is methyl or ethyl when faced with the prior art of Del Soldato. Del Soldato discloses the compounds, such as example 14, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato et al. (WO 95/30641).

Determining the scope and contents of the prior art

Del Soldato et al. discloses the compounds of formula A-X1-NO₂ (page 6) which have anti-inflammatory and analgesic activity (page 1) such as the compound of the formula of Example 1b (page 43):

2-{N-[2,6-(dichloro)phenyl]amino}phenylacetate of 2-[2-(nitroxy)ethoxy]ethyl



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

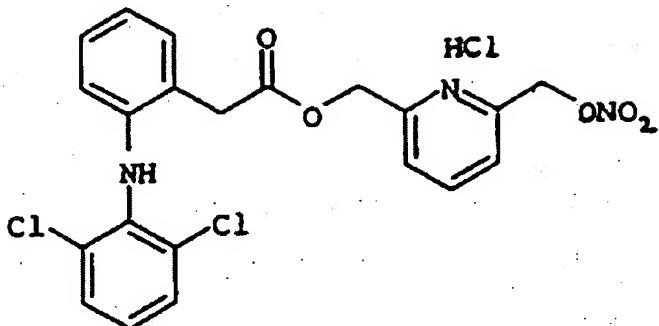
However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Del Soldato et al. Del Soldato et al. discloses the compounds, such as the formula of example 1b, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent

unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benedini et al. (WO 2000051988).

Determining the scope and contents of the prior art

Benedini et al. discloses the compounds of formula A-X1-N(O)_z (page 4) which have anti-inflammatory and analgesic activity (page 1) such as the compound of the formula of Example 13 (page 46):



Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

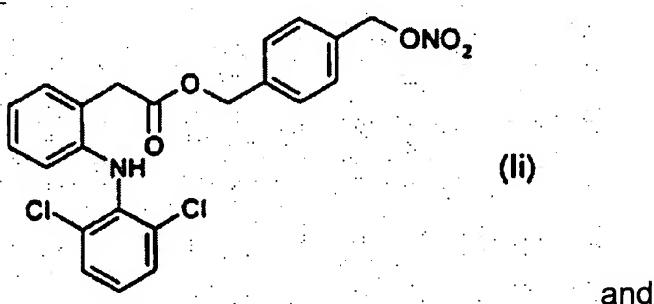
However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Benedini et al. Benedini et al. discloses the compounds, such as example 13, which are useful as anti-inflammatory agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an

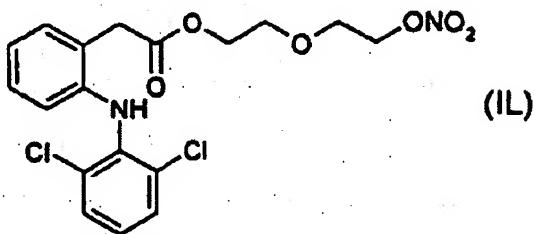
advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as anti-inflammatory agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eek et al. (WO 2000072838).

Determining the scope and contents of the prior art

Eek et al. discloses the compounds of the formula (I), M-C(=O)-O-X-ONO₂ on page 3 which are useful as antibacterial agents (page 1). Specific compounds of formula (I) are found on pages 6 (formula II) and 7 (formula I_L):





Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art has a hydrogen atom at the position equivalent to applicants R4 instead of a methyl or ethyl.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare applicants' elected invention wherein R4 is methyl or ethyl when faced with the prior art of Eek et al. Eek et al. discloses the compounds of formula (I) such as (ii) and (IL) which are useful as antibacterial agents which differ from applicants' elected invention only by having a hydrogen in position R4. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity. Furthermore, To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in

adjacent members. *In re Henze*, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as antibacterial agents. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Rebecca Anderson
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Art Unit 1626, Group 1620
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March 29, 2006